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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,705	02/25/2002	Ulrich Noth	NOT01-NP002	5327
7590	05/06/2004		EXAMINER MARVICH, MARIA	
David S. Resnick NIXON PEABODY LLP 100 Summer Street Boston, MA 02110			ART UNIT 1636	PAPER NUMBER

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,705	NOTH ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 15,16,18-20 and 23-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14,17,21 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 2/25/02 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/16/02</u> . | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> . |

Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

DETAILED ACTION

This office action is in reply to a response to a Restriction Requirement filed 4/12/2003. Claims 1-28 are pending in this application.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-14, 17 and 21-22) in the Amendment filed 4/12/03 is acknowledged. Claims 15-16, 18-20 and 23-28 are withdrawn from consideration as being drawn to nonelected subject matter.

Information Disclosure Statement

An IDS filed 12/16/02 has been identified and the documents considered. The signed and initialed PTO Form 1449s have been mailed with this action.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. A statement did not accompany the submission of the substitute Paper Copy and Computer Readable Form of the Sequence listing, filed 2/25/02, that the substitute sequence listing did not contain New Matter. Applicant must provide a substitute computer readable form (CRF), paper copy of the

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“Sequence Listing” and a statement that the CRF and “Sequence Listing” are the same and contain no New Matter.

Drawings

The drawings are objected to because in figure 3, figure 3A is either not labeled or the label is obscured by the details of the photograph.

Specification

The disclosure is objected to because of the following informalities: the brief description to the drawings for figure 4 includes a description of figures 4k and 4l. However, there are no such panels in the figure.

Appropriate correction is required.

Claim Objections

Claim 1 is objected to because of the following informalities: MSCs is abbreviated without defining it, the first occurrence of MSCs should be accompanied by the definition. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-14, 17 and 21-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and by dependency claims 2-14 are vague and indefinite in that the metes and bounds of “a top surface” are unclear. It is not clear how to determine which surface is the “top surface”. The specification states that the matrix block may be any shape or size that is compatible with the cartilage defect site. There are several shapes for which designation of a “top surface” is impractical. As the surface that the cells are press-coated to is specifically limited to the top, it would require knowing how to distinguish the top surface.

Claims 10, 12 and 13 and by dependency claims 11 and 14 are vague and indefinite in that the metes and bounds of “to elicit osseointegration” are unclear. Use of the word “elicit” is confusing as it is unclear how osseointegration is or can be “elicited”.

Claim 12 recites the limitation “the remaining volume” in claim 1. There is insufficient antecedent basis for this limitation.

Claim 13 is vague and indefinite in that the metes and bounds of the graft further comprising an osteoinductive growth factor to elicit osseointegration are unclear. Claim 13 is dependent from claim 12 in which the graft is comprised of a second population of MSC that already elicit osseointegration.

Claim 17 and by dependency 21-22 are vague and indefinite in that the metes and bounds of the “cell-matrix structure” are unclear. Neither the specification nor the prior art define a “cell-matrix structure”.

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Claim 17 is vague and indefinite in that the metes and bounds of “a high-density pellet” are unclear. The specification teaches an embodiment in which the cell pellet comprises $1-2 \times 10^6$ cells. Specifically, it is stated that 1.5×10^6 cells formed a formed cell pellets that were 2 mm in height at the bottom of a 5 ml tube. It is not clear if these specifically define a “high-density pellet” or are just a single example.

Claim 17 is vague and indefinite in that the metes and bounds of “first period of time” and “second period of time” are unclear. The specification teaches an embodiment in which the first period is 3 hours and the second period is 3 weeks. It is not clear if this defines the first and second periods of time or is just a single example of the times.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim an engineered osteochondral graft that further comprises an osteoinductive growth factor.

The written description requirement for a genus claim may be satisfied through sufficient description of a relevant a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics such as structure or

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other physical and/or chemical properties, by functional characteristics couple with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus.

In the instant case, applicants only disclose that BMP-2 is an osteoinductive growth factor that can be included in the graft. This recitation is not accompanied by a disclosure as to the additional growth factors that might constitute osteoinductive growth factors or the relative properties of growth factors that make them osteoinductive. Therefore, there is no clear description of the structural or functional characteristics required for an osteoinductive growth factor. Given the large size and diversity of growth factors and the inability to envision which will also be osseointegrative, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Valentini and Kim (US 5,939,323; see entire document).

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Valentini and Kim teach the development of scaffolds that are useful for a variety of medical purposes (see e.g. abstract). The scaffold is comprised of porous biodegradable polymers such as polylactic acid and can be any size or shape depending upon the application (see e.g. column 1, line 64 through column 2, line 10 and column 6, line 40-47). The scaffold is not limited to any particular shape but is designed to meet the needs of the medical procedure for example to repair cartilage defects (see e.g. column 7, line 46-48). The scaffold serves as a substrate for cells such as mesenchymal stem cells from bone marrow and periosteum and endosteum (see e.g. column 7, line 35-42). Cells are contacted with the scaffold and permitted to grow upon and/or into the pores of the scaffold. As the technique of press-coating is not defined or described in the specification of the instant invention, it is unclear that *contacting the surface of the scaffold with the cells* does not entail press-coating. Cells were seeded on the scaffold for 30 minutes (first time period) and then grown for 11 weeks (second time period). Additionally included in the scaffold is BMP-2 (see e.g. column 13, line 5-14).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valentini and Kim (US 5,939,323; see entire document) in view of Brekke and Toth (J

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Biomed Mater Res 43:380-398, 1998; see entire document) and Hung and Lo (US 2002/0045260; see entire document).

Applicants claim engineered osteochondral graft made of D,D-L,L-polylactic acid and a method of making the graft in which a high-density pellet of MSC are grown for a first and second time in chondrogenic differentiation medium.

The teachings of Valentini and Kim are described above and are applied as before except:

Valentini and Kim do not teach use of D,D-L,L-polylactic acid in the matrix or a method of making the graft in which a high-density pellet of MSC are grown for a first and second time in chondrogenic differentiation medium.

Brekke and Toth teach devices for tissue engineering which are comprised of D,D-L,L-polylactic acid.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute polylactic acid taught by Valentini and Kim with the D,D-L,L-polylactic acid taught by Brekke and Toth because Valentini and Kim teach that it is within the ordinary skill of the art to make a scaffold comprised of biodegradable polymers and because Brekke and Toth teach that it is within the ordinary skill of the art to use D,D-L,L-polylactic acid in tissue engineering. One would have been motivated to do so in order to receive the expected benefit of a scaffold that can be molded into three-dimensional architecture to deliver compounds such as cells or BMP2 to subjects and that satisfy performance criteria (see Brekke and Toth, page 393, paragraph 2 and page 390, paragraph 3 and 4). Based upon the teachings of the cited references, the high skill of

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one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims allowed.

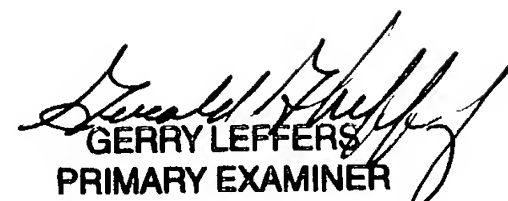
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

April 29, 2004


GERRY LEFFERS
PRIMARY EXAMINER